

Appln. No. 10/658,617  
Reply to Office action of June 1, 2005  
Response dated October 3, 2005

**AMENDMENT(S) TO THE DRAWING(S)**

The attached sheets of drawings include changes to Figs. 3, 7, 10, 12, 15, and 25B. These sheets, which includes Figs. 3, 7, 10, 12, 15, and 25B, replaces the original sheet.

Attachment: Replacement Sheet

**REMARKS**

**I. Introduction**

This paper is submitted in response to the Office Action mailed June 1, 2005 for the above-identified patent application. Claims 1-27 are pending in the application. Claims 13-18 are allowed. Claims 1-12 and 19-27 have been rejected.

The Examiner states that the application discloses a nucleotide sequence but the application does not contain a sequence listing. Applicants submit herewith a sequence listing in compliance with 37 CFR §§1.821-1.825 to satisfy the requirements for patent applications containing sequence disclosures.

Applicants submit herewith an initial Sequence Listing in computer and paper form, in accordance with 37 C.F.R. §1.821-1.825. The content of the paper and computer readable copies of the Sequence Listing submitted in accordance with 37 C.F.R. §1.821(c) and (e) are the same and do not include new matter.

Amendments have been made to the specification to insert sequence identifiers. Applicants also submit herewith replacement sheets of Figs. 3, 7, 10, 12, 15, and 25B to include sequence identifiers. Applicants submit that no new matter has been introduced by the amendments to the specification. Support for the amendments is found in the specification and claims as originally filed.

The Examiner notes that the Applicants have claimed priority from prior application nos. 10/374,784 and 60/359,948 in the Declaration and transmittal papers, but have not made reference to the priority data in the specification. Therefore, Applicants

amend the first page of the specification to recite that the present application is a continuation-in-part of U.S. patent application 10/374,784 filed February 25, 2003, now pending, which claims benefit of provisional application 60/359,948, filed February 25, 2002.

**II. The Obviousness-Type Double Patenting Rejection Should Be Withdrawn**

The Examiner has provisionally rejected claims 1-12 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7, 11-13, 16-17, 27, 29-33 of copending Application No. 10/374,784 (“the ‘784 application”). The Examiner states that the claims are generic in that they recite that the sequence to be trans-spliced to the target pre-mRNA encodes a light producing protein or enzyme, while the claims in the ‘784 application recite that the sequence to be trans-spliced encodes a molecule which provides a fluorescent or bioluminescent signal.

Applicants have amended independent claims 1, 3, 5, 7, 9 and 11 to recite that the light producing protein or enzyme activates a cytotoxic photosensitizer that causes cell death. In contrast, the claims of the ‘784 application recite that the nucleotide sequence encodes a reporter molecule. Therefore, reconsideration and withdrawal of the rejection of claims 1-12 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the ‘784 application is respectfully requested.

The Examiner has rejected claims 19-26 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11, 25-32, 46-55 and 84-93 of copending Application No. 10/434,727 to Otto (“the ‘727 application”).

The Examiner states that the claims are generic in that they recite that the sequence to be

trans-spliced to the target pre-mRNA encodes a adenoviral protein or a polypeptide which function as a light inducing enzyme or protein, while the '727 application claims a nucleotide sequence that encodes an adenovirus protein.

Applicants have amended independent claims 19, 21, 23 and 25 to remove recitation to adenoviral polypeptide. Thus, as presently amended the claimed invention recites a nucleotide sequence that encodes a light producing protein or enzyme. In contrast, the claims of the '727 application recite that the nucleotide sequence encodes an adenovirus protein. Therefore, reconsideration and withdrawal of the rejection of claims 19-26 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the '727 application is respectfully requested.

### **III. The Rejections Under 35 U.S.C. §102/103 Should Be Withdrawn**

The Examiner has rejected claims 1-12 under 35 U.S.C. §102(e) as anticipated by the '784 application. The Examiner has also rejected claims 1-12 under 35 U.S.C. §103(a) relying on the '784 application qualifying as prior art under 102(e). The Examiner alleges that the first disclosure of the claimed subject matter is in the present application and, therefore, is only entitled to a filing date of September 9, 2003, rather than the filing date of the '784 application (*i.e.*, February 25, 2003) or the filing date of provisional application 60,359,948 (*i.e.*, February 25, 2002).

Applicants respectfully disagree. The present invention provides methods and compositions for conferring selective death on cells expressing a specific target precursor messenger RNA (selective target pre-mRNAs). The compositions of the invention include pre-trans-splicing molecules (PTMs) designed to interact with one or more

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selective target pre-mRNA and mediate a trans-splicing reaction resulting in the generation of novel chimeric mRNA molecules (chimeric mRNA) capable of encoding light producing proteins or enzymes. The light producing proteins include those capable of fluorescence, fluorescent resonance energy transfer, and phosphorescence.

Provisional application 60/359,948, filed February 25, 2002, from which the present application claims priority, discloses that PTMs may be engineered to contain any nucleotide sequence encoding a protein product that functions as a reporter molecule. The reporter molecule includes, but is not limited to, fluorescent and bioluminescent molecules. Bioluminescent molecules include, *e.g.*, firefly, Renilla or bacterial luciferase. Fluorescent molecules include, *e.g.*, green fluorescent protein or red fluorescent protein. *See* Provisional Application 60/359,948, paragraphs 30 and 43; and Section 6.1.3. Therefore, it is respectfully submitted that the subject matter claimed in the present invention, which comprises a nucleotide sequence encoding a light producing protein or enzyme to be trans-spliced to a target pre-mRNA, is entitled to the filing date of provisional application 60,359,948 (*i.e.*, February 25, 2002).

Furthermore, Applicants have amended independent claims 1, 3, 5, 7, 9 and 11 to recite that the light producing protein or enzyme activates a cytotoxic photosensitizer that causes cell death. Therefore, reconsideration and withdrawal of the rejection of claims 1-12 under 35 U.S.C. §§102(e) and 103(a) as unpatentable over the '784 application is respectfully requested.

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The Examiner has rejected claims 19-26 under 35 U.S.C. §102(e) as anticipated by the '727 application. The Examiner has also rejected claims 19-26 under 35 U.S.C. §103(a) relying on the '727 application qualifying as prior art under 102(e).

As stated above, it is respectfully submitted that the claimed subject matter is entitled to the filing date of provisional application 60,359,948 (*i.e.*, February 25, 2002). Therefore, the '727 application is not prior art to the present application. Moreover, Applicants have amended independent claims 19, 21, 23 and 25 to recite that the nucleotide sequence encodes a light producing protein or enzyme. Therefore, reconsideration and withdrawal of the rejection of claims 19-26 under 35 U.S.C. §§102(e) and 103(a) as unpatentable over the '727 application is respectfully requested.

#### **IV. The Rejections Under 35 U.S.C. §112 ¶2 Should Be Withdrawn**

The Examiner has rejected claim 27 under 35 U.S.C. §112 ¶2 as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regard as the invention. In particular, the Examiner states that there is no antecedent basis for the term "the conditionally replicative adenovirus." Applicants have amended claim 27 to overcome the rejection.

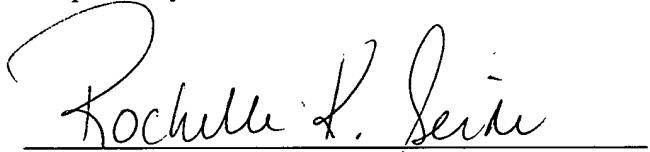
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V. **Conclusion**

In view of the foregoing remarks, reconsideration and allowance of the pending claims is respectfully requested.

A one (1) month extension to the time for responding to the Official Action is respectfully requested. Payment of the extension fee is to be made according to the Credit Card Payment Form attached herewith. Applicants believe that no additional fees are required in connection with this response. However, if additional fees are required, the Commissioner is hereby authorized to charge any additional payment, or credit any overpayment, to Deposit Account No. 01-2300, **referencing Docket Number 027705.00026.**

Respectfully submitted,



Rochelle K. Seide, Ph.D.  
Registration No. 32,300  
ARENT FOX PLLC  
1675 Broadway  
New York, NY 10019  
Tel. No. (212) 484-3945  
Fax No. (212) 484-3990  
Customer No. 38485

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### **FEE CALCULATION**

Any additional fee required has been calculated as follows:

If checked, "Small Entity" status is claimed.

	(Column 1)	(Column 2)	(Column 3)
	CLAIMS REMAINING AFTER AMENDMENT	HIGHEST NO. PREVIOUSLY PAID FOR	PRESENT EXTRA
TOTAL CLAIMS	61 MINUS	65	= -0-
INDEP CLAIMS	16 MINUS	16	= -0-
<input type="checkbox"/> FIRST PRESENTATION OF MULTIPLE DEP. CLAIM			

#### **SMALL ENTITY**

RATE	ADD'L FEE
x \$25	\$0.00
x \$100	\$0.00
+ \$180	\$0.00

OR

#### **LARGE ENTITY**

RATE	ADD'L FEE
x \$50	\$
x \$200	\$
+ \$360	\$

The U.S. Patent and Trademark Office is hereby authorized to charge and deficiency or credit any overpayment of fees associated with this communication to Deposit Account No. 01-2300 referencing docket number 027707.00026.